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(54) Title: NOVEL COMPOSITION

(57) Abstract: An oral care composition comprising a dispersion of responsive or non-responsive microgel particles, and at least one orally acceptable carrier or excipient for treating dentine hypersensitivity. Microgel particles comprise a polymeric network comprising monomeric units interconnected with one another through a crosslinking agent in which the polymeric network can be obtained by polymerization in a dispersed medium of a suitable monomer e.g. a vinyl monomer, and a crosslinking agent.



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Novel Composition

Field of the Invention

The present invention relates to oral care compositions comprising certain
5 microgels and their use in combating dentine hypersensitivity.

Background of the Invention

Dentine hypersensitivity is a common but painful condition affecting 18-42% of the adult population and has been defined as “short, sharp pain arising from exposed dentine in
10 response to stimuli, typically thermal cold, evaporative, tactile, osmotic or chemical which cannot be ascribed to any other form of dental defect or pathology” (*Int. Dent. J.* 2002; 52: 367-375). The primary origin is generally agreed to result from the exposure of dentine following either loss of the protective enamel layer or via gum recession.

The most pronounced morphological characteristic of human dentine is its tubular
15 structure. Dentine tubules have diameters on the order of several micrometers and connect the pulp to the enamel dentine junction. In a healthy subject, these tubules are filled with fluid. It is postulated that this dental fluid plays an active role in the transmission of pain stimuli across the dentine to the underlying neurons. This widely-accepted theory, known as the hydrodynamic theory, states that when the dentine tubules become exposed to the
20 environment, external stimuli elicit a displacement of the dentinal fluid, which, in turn, stimulates mechanoreceptors in the pulp. The movement of fluid through the narrow tubules irritates cells in the vicinity of the base of the tubules, including odontoblasts, pulpal neurons, and even subodontoblastic blood vessels. Several researchers have shown that the fluid movements result in the release, from the pulpal nerves, of calcitonin gene-
25 related peptide, which generates a local neurogenic inflammatory condition.

There are two categories of therapy for the treatment of dentine hypersensitivity based upon two modes of action. The first category, nerve-depolarising agents, comprises pharmaceutical agents such as potassium nitrate which function by interfering with neural transduction of the pain stimulus.

30 The second category, known as occluding agents, function by physically blocking the exposed ends of the dentinal tubules, thereby reducing dentinal fluid movement and reducing the irritation associated with the shear stress described by the hydrodynamic theory.

The occlusion approach typically involves treating the tooth with a chemical or physical agent that creates a deposition layer within or over the dentine tubules. This layer mechanically occludes the tubules and prevents or limits fluid movement within the tubule to such an extent that stimulation of the neuron is not achieved. Examples of occlusion
5 actives include among others, calcium salts, oxalate salts, strontium salts, stannous salts, glasses, inorganic oxide particles e.g. SiO_2 , Al_2O_3 and TiO_2 and polymer e.g. methylmethacrylate based varnishes.

US 5,270,031 (Block) relates to water soluble or water swellable polymers with functional groups that are capable of bearing one or more charged groups in an aqueous
10 solution having desensitising properties. Such polymers can be anionic, cationic or amphoteric. One example of an anionic functional group is the carboxylate group which is found in polymers such as polyacrylic acid, copolymers of acrylic acid and maleic acid, copolymers of methacrylic acid and acrylic acid, and copolymers of alkyl vinyl ethers and maleic acid or anhydride.

15 US 5,885,551 (Block) relates to a method of treating dentinal hypersensitivity by administering alginic acid or an alginate in an oral care composition.

US 6,096,292 (Block) relates to the use of a superabsorbent acrylic polymer as a desensitising agent.

US 6,241,972 (Block) relates to compositions and their use in treating dentinal
20 hypersensitivity comprising a copolymer having repeated units of a hydrophilic monomer such as a carboxylic acid, a dicarboxylic acid or a dicarboxylic acid anhydride and a hydrophobic monomer consisting of an alpha-olefin having at least eight carbon atoms, full and partially hydrolysed forms thereof and full and partial salts thereof. A preferred desensitising agent is PA-18 which is an alternating copolymer of a 1:1 molar ratio of
25 maleic anhydride and 1-octadecene.

Despite the above proposals, there remains a need for alternative treatments for alleviating dental hypersensitivity.

Microgel technology utilises microgel particles comprising particles formed of a network of crosslinked polymers which, in a given solvent such as water at room
30 temperature, can exist in a swollen or a collapsed conformation. In response to an external stimulus such as temperature, pH or ionic strength, microgel particles have been shown to shrink or swell reversibly as a result of an increase or decrease in solvent quality (Saunders B. R., Vincent B., Advances in Colloid and Interface Science, 80 (1), 1999, 1-25).

The extent to which the network of crosslinked polymeric particles is expanded by solvent depends on the conformational state of the microgel particles. When the particles are in a swollen state, the polymer-solvent interactions typically are strong with the polymer chains being fully solvated and the interstitial regions between polymer chains being occupied by solvent. However even in the collapsed state, microgel particles have been reported to retain a large amount of “structural” solvent, typically water. In view of their “sponge-like” properties, microgel particles have been proposed for use in a number of industries including the surface coating and printing industries as well as the pharmaceutical industry.

GB 2 431 104 A (University of Greenwich) proposes a device comprising microgel particles grafted to a substrate. The device is particularly intended for use as a wound dressing.

WO03/082316 (Regents of the University of California) discloses microgels as delivery agents, capable of delivering bioactive materials to cells for use as vaccines or therapeutic agents.

JP2005104966 (Lion Corporation) describes, for oral application, compositions containing one or more gelling agents selected from agar, gallant gum, carrageenan, pectin and sodium alginate, and a cross-linking agent for crosslinking the gelling agents wherein the composition contains microgel particles having an average particle diameter of not less than 0.01 μ m and less than 1,000 μ m and further has a viscosity of 1 to 5,000 mPa*s at 25°C.

WO2008/145612 (Universidad Del Pais Vasco) describes pharmaceutical compositions comprising biocompatible microgels and their use in transporting and dosing biologically active agents.

EP 0 721 773 (Sun Medical Co. Ltd) describes compositions for relieving dentine hypersensitivity comprising (A) an aqueous emulsion component (1) containing polymer particles as emulsion particles having a diameter smaller than that of a dentinal tubule and forming an agglomerate larger than the diameter of a dentinal tubule when they react with a calcium compound and (2) which has a metal ion concentration in a dispersing medium of 1,000 ppm or less and (B) a water soluble organic component or a water-soluble salt component thereof, a calcium salt of the organic acid being insoluble or hardly soluble in water. According to EP 0 721 773 a small sized emulsion particle penetrating into a dentine tubule reacts with a calcium ion eluted from hydroxyapatite present in dentin that

forms the dentinal tubules or a calcium ion present in a marrow liquid contained in dentine to form a great number of agglomerates, which are then laid continuously in the longitudinal directions of the dentinal tubules as a coating film.

5 **Brief Description of the Drawings**

Figure 1. % of transmitted light at 547 nm vs temperature for ◆ poly(NIPAM/AAc) and ◇ poly(NVCL/MMA)

Figure 2. First derivative of transmitted light at 547 nm vs temperature for ◆ poly(NIPAM/AAc) and ◇ poly(NVCL/MMA)

10 **Figure 3.** Hydrodynamic diameter of microgel particles vs. temperature by DLS, ◆ poly(NIPAM/AAc) and ◇ poly(NVCL/MMA)

Figure 4. Hydrodynamic diameter of poly(NIPAM/AAc) microgel particles vs. pH by DLS

Figure 5. Bovine dentine treated with poly(NIPAM/AAc), 2 wt %, (HC Method One)

15 **Figure 6.** Bovine dentine treated with poly(MMA/MAAc), 2 wt %, (HC Method One)

Figure 7. Bovine dentine treated with poly(NIPAM/AAc), 2 wt % (HC Method Two)

Figure 8. Bovine dentine treated with poly(NVCL/MMA), 0.5 wt % (HC Method Two)

Detailed Description of the Invention

20 The present invention is based on the discovery that certain microgels provide tubule occluding properties and have been shown to reduce dentine permeability in the industry standard hydraulic conductance (Hc) model. This model is a well recognized and accepted model for anti-sensitivity agents whose mode of action is based on tubule occlusion (Outhwaite, W.C et al (1974), A Versatile Split chamber Device for Studying
25 Dentine Permeability. Journal of Dental Research, 57, 1503).

Accordingly in a first aspect of the invention there is provided an oral care composition comprising a dispersion of responsive or non-responsive microgel particles, and at least one orally acceptable carrier or excipient for treating dentine hypersensitivity and wherein the responsive microgel particles undergo a physical conformational change
30 in response to a trigger selected from temperature and/or pH.

An oral care composition of the invention is a dentinal composition, preferably in the form of a dentifrice or a mouthwash. Microgel particles of use in the present invention comprise a polymeric network comprising monomeric units interconnected with one

another through a crosslinking agent in which the polymeric network can be obtained by polymerisation in a dispersed medium of a suitable monomer e.g. a vinyl monomer, and a crosslinking agent. In contrast to the compositions described in EP 0 721 773, a composition of the present invention does not require the presence of a water-soluble organic acid component or a water-soluble salt component thereof wherein the calcium salt of the organic acid component is insoluble or hardly soluble in water. Accordingly inclusion of such a component is entirely optional. In one aspect a composition of the present invention does not comprise such a component.

Microgel particles of use in the invention comprise generally spherical discrete cross-linked polymeric particles, which, when in the swollen state are in the size range of about 50 nm to about 2 microns, and in the collapsed state are in the size range of about 1 nm to about 500 nm. It is understood that different microgel particles will comprise different size ranges in the collapsed and swollen states and may overlap in size ranges. Notwithstanding this, it is believed that the microgel particles of use in the invention are capable of penetrating and occluding the dentinal tubules, both in the swollen and in the collapsed state.

Suitably in one embodiment the size range of the microgel particles in the swollen state is from about 0.1 micron to about 1 micron diameter more particularly from 0.40 micron to about 0.90 micron diameter. Suitably in one embodiment the size range of the microgel particles in the collapsed state is from about 50 nm to about 400 nm. Particle size may be controlled by a variety of parameters known in the polymer art such as the number and concentration of reactants such as monomer, cross-linker and initiator, polymerisation reaction conditions, e.g. stirring speed and reaction temperature, and use of particular additional reagents e.g. surfactants.

Microgel particles are suitably provided for formulation in an oral care composition according to the invention in the form of a microgel dispersion (also known as a microgel). A microgel dispersion as referred to herein is a two-phase system consisting of a dispersed phase, comprising cross-linked polymeric particles, uniformly dispersed throughout a medium, typically water. Alternatively the microgel particles may be provided in a dry form e.g. in the form of a spray dried powder, and then re-hydrated suitably in an aqueous medium prior to or during formulation of the oral care composition.

Microgel particles for use in the invention are distinguished from superabsorbent polymers (SAPs) known in the art, for example as described in US 6,096,292 (Block).

SAPs comprise extremely large liquid-absorbing and liquid-retaining capabilities and have a high gelling capacity or swelling ratio e.g. in the region of 1000:1. In contrast the microgel particles used herein comprise a relatively low gelling capacity or swelling ratio e.g. in the region of from about 75:1 to about 300:1, preferably about 100:1 to about 150:1.

5 Microgel particles of use herein may be responsive or non-responsive. In one embodiment the microgel particles are responsive. Responsive microgel particles as referred to herein are microgel particles that undergo a reversible or non-reversible physical conformational change, for example in the oral cavity, in response to a relevant trigger selected from temperature and/or pH.

10 Following exposure to the relevant trigger, the physical conformational change in the microgel particles typically occurs rapidly. Ideally the responsive microgel particles of use in the invention comprise a very high polymer surface area to particle volume ratio which allows a rapid diffusion of a given stimulus thereby allowing a quick response throughout the entire microgel matrix, typically of the order of a few seconds.

15 In one aspect the physical conformational change comprises a reversible or non-reversible volume phase transition. The volume phase transition may result in significant changes in particle radius and surface area, internal particle volume, and surface charge density. For example, microgel particles formed of poly N-isopropylacrylamide (poly-NIPAM) are known having a collapsed particle size of 240 nm and a swollen particle size
20 of 450 nm (M.J. Snowden, B. Vincent, J. Chem. Soc. Chem. Commun, 1992, 1103-1105).

 Whilst not being bound by any particular theory, it is believed that the occlusional properties of responsive microgel particles are facilitated or enhanced following a physical conformational change of the said particles. For example it is believed that dentinal tubules become physically blocked, for example, with either swollen microgel particles or
25 collapsed (i.e. shrunken) particles which then flocculate following an appropriate volume phase transition. It is believed that the aggregation (flocculation) of the microgel particles takes place as a result of a DLVO mechanism. This involves the van der Waals attractive force between the particles increasing as the microgel particles shrink. As the particles are dispersed in electrolyte the attractive force on shrinking becomes greater than the repulsive
30 force originating from a surface charge on the microgel particles, and hence the particles aggregate.

 In one embodiment the responsive microgel particles undergo a volume phase transition in the oral cavity from a swollen state to a collapsed state, followed by

flocculation of the collapsed particles. In an alternative embodiment, the responsive microgel particles undergo a volume phase transition in the oral cavity from a collapsed state to a swollen state.

In one aspect the trigger is temperature and the physical conformational change is a volume phase transition occurring at the volume phase transition temperature (VPTT) of the responsive microgel particles. By “volume phase transition temperature” is meant the temperature at which the responsive microgel particles undergo a volume phase transition.

Microgel particles that are triggered by temperature may be referred to herein as thermally responsive microgel particles. Thermally responsive microgel particles useful in the invention are those that undergo a reversible volume phase transition at a volume phase transition temperature in the range from about 30°C to about 50°C, for example in the normal temperature range of the oral cavity, suitably from about 32°C to about 38°C, or a range above the normal temperature of the oral cavity for example from about 39°C to about 45°C. The VPTT of a microgel dispersion may be quoted as a single temperature value or a temperature range. The VPTT of the microgel particles may be determined by methods known in the art e.g. by turbidimetric analysis utilizing ultra violet-visible spectroscopy, for example where percentage transmission is measured at a wavelength of 547nm as a function of temperature. Suitably thermally responsive microgel particles of use in the invention are in the swollen state at temperatures below the VPTT and are in the collapsed state at temperatures above the VPTT.

In one embodiment an oral composition according to the invention comprises thermally responsive microgel particles having a VPTT in the region of the temperature of the oral cavity e.g. in the range from about 32°C to about 38°C. In this embodiment the composition is applied at a temperature below the VPTT of the microgel particles, for example at about room temperature e.g. in the range from about 20°C to about 25°C. As the temperature of the composition is heated, typically *in situ* i.e. in the oral cavity, and equilibrates with that of its environment, the microgel particles undergo a volume phase transition at the VPTT from the swollen state to the collapsed state i.e. the microgel particles shrink in size, which is followed by flocculation of the collapsed particles.

Accordingly in one aspect of the invention there is provided an oral care composition wherein the microgel particles are thermally responsive having a VPTT in the range from about 32°C to about 38°C, such that suitably on application of the composition to the oral cavity, the microgel particles undergo a volume phase transition in the oral

cavity. In this aspect the microgel particles can undergo a volume phase transition from a swollen state to the collapsed state, followed by flocculation.

Alternatively, in one embodiment, an oral composition according to the invention comprises thermally responsive microgel particles having a VPTT above the temperature of the oral cavity i.e. greater than about 38°C e.g. in the range from about 39°C to about 45°C. On heating such a composition to the VPTT or beyond, for example to above 45°C, the microgel particles undergo a reversible first volume phase transition i.e. from a swollen state to a collapsed state. Such heating may occur *in situ* in the oral cavity e.g. via an exothermic reaction such as hydration of magnesium chloride, or more suitably prior to application of the composition to the oral cavity e.g. in a suitable oven e.g. a microwave oven. In use the composition is cooled to the ambient surrounding temperature of the oral cavity, and the microgel particles therein undergo a second volume phase transition i.e. from the collapsed state to the swollen state, as the temperature falls below the VPTT. In such an embodiment it is the swollen microgel particles that block the dentine tubules.

Accordingly in one aspect of the invention there is provided an oral care composition wherein the microgel particles are thermally responsive and have a VPTT which is higher than the temperature of the oral cavity e.g. in the range 39°C to 45°C, such that on heating the composition to the VPTT or above, the microgel particles undergo a reversible first volume phase transition, and then on cooling to below the VPTT, suitably in the oral cavity, the particles undergo a second volume phase transition. In this aspect the first volume phase transition of the microgel particles is from the swollen state to the collapsed state, and the second volume phase transition of the microgel particles is from the collapsed state to the swollen state. Counter-intuitively there is a decrease in particle size with an increase in temperature, and vice versa, i.e. there is an increase in particle size with a decrease in temperature.

In an alternative aspect the environmental condition that prompts a physical conformational change is pH. When pH is the trigger, useful microgels are those that undergo a volume phase transition and have a volume phase transition pK_a (VPpK_a) at a pH in the range from about 4.5 to about 8.0. This pH range reflects the distribution of oral mucosal pH values in a healthy subject, however when the pH drops to below pH 5.5 it is potentially harmful to enamel and dentin. In order to maintain a non-harmful pH in the oral cavity the salivary system employs various buffers, which maintain a pH of from about 6.0 to about 7.5.

Suitably the $VPpK_a$ may be determined by methods known in the art e.g. by turbidimetric analysis utilizing ultra violet/ visible spectroscopy, for example where percentage transmission is measured at a wavelength of 547nm as a function of pH.

Accordingly in one aspect according to the invention there is provided an oral care
5 composition wherein the microgel particles are responsive to pH having a $VPpK_a$ at a pH in the range 4.5 and 8.0, such that following application of the composition suitably to the oral cavity the microgel particles undergo a volume phase transition in the oral cavity.

In one embodiment, an oral care composition according to the invention comprises microgel particles that are pH responsive having a $VPpK_a$ above the pH of the oral cavity
10 i.e. greater than pH 7.0 e.g. pH 7.5. One application of such a composition may involve formulating the composition at pH greater than the $VPpK_a$, for example at pH 8.0, where, suitably, the microgel particles are in a swollen state. On application to the oral cavity the pH of the composition is lowered to the ambient surrounding pH of the oral cavity (~pH 7.0), and the microgel particles undergo a volume phase transition, for example going from
15 a swollen state to a collapsed state and flocculating as the pH falls below the $VPpK_a$ and thereby facilitating or enhancing the occluding properties of the microgel particles.

In an alternative embodiment an oral care composition according to the invention comprises microgel particles that are pH responsive having a $VPpK_a$ at the pH of the oral cavity, for example at about pH 7.0. One application of such a composition may involve
20 formulating the composition at a pH below the $VPpK_a$, e.g. in the range of pH 4.5 to 6.5, for example pH 6.0, so that the microgel is in a collapsed state. On application to the oral cavity the pH of the composition is raised to the ambient surrounding pH of the oral cavity (~pH 7.0), and the microgel particles undergo a volume phase transition, for example going from a collapsed state to a swollen state as the pH rises above the $VPpK_a$.

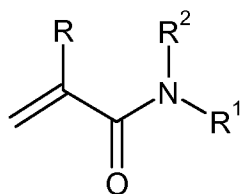
25 One further aspect according to the invention utilises non-responsive microgel particles. Non-responsive microgel particles, as referred to herein, are those microgel particles that do not undergo a conformational change in the oral cavity, yet nevertheless comprise tubule occluding properties. Whilst it is not to say that under certain circumstances, such particles cannot be triggered to undergo a conformational change, the
30 tubule occluding properties of non-responsive microgel particles referred to herein are believed to be achieved by a different mechanism(s) e.g. via chemical interaction of the particles with dentine/enamel and/or tubular fluid.

Accordingly in one such aspect according to the invention there is provided an oral care composition comprising non-responsive microgel particles, and at least one orally acceptable carrier or excipient.

One aspect according to the invention utilises microgel particles which may be responsive or non-responsive which comprise surface groups of opposing charge. These particles comprise tubule occluding properties via a heteroflocculation mechanism which is believed to occur through electrostatic attraction of opposing charges.

Microgel particles for use in the invention comprise at least one monomer, a radical reaction initiator and suitably a cross-linking agent, and may be prepared by methods known in the polymer art e.g. by polymerising or copolymerising suitable monomer or monomers in the presence of a free radical initiator and a cross-linking agent. For purposes herein, the term “homopolymer microgel” refers to a microgel derived from a single monomer (excluding a cross-linking monomer) and the term a “co-polymer microgel” refers to a microgel prepared from two or more different monomers (excluding a cross-linking monomer). Monomers useful in the preparation of thermally or pH responsive or non-responsive homo or co-polymer microgels comprise one or more monomers selected from monomers A, comprising A1 to A5 below, and/or monomers B, comprising B1 to B2 below:

A1. Vinyl amides of Formula (I)

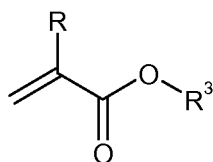


Formula (I)

wherein R is H or C₁-C₆ alkyl, and R¹ and R² which may be the same or different are selected from H or C₁-C₆ alkyl optionally substituted by hydroxy or C₁-C₆ alkoxy.

Examples of a monomer of Formula (I) include N-ethylacrylamide, N-isopropylacrylamide and N,N-dimethylacrylamide;

A2. Vinyl esters of Formula (II)

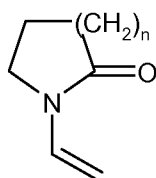


Formula (II)

wherein R is as hereinbefore defined and R³ is C₁-C₆ alkyl substituted by hydroxy.

- 5 Examples of a monomer of Formula (II) include hydroxyethyl acrylate, hydroxyethyl methacrylate, hydroxylpropyl acrylate, hydroxypropyl methacrylate and hydroxybutyl acrylate;

A3. N-vinyl lactams of Formula (III)

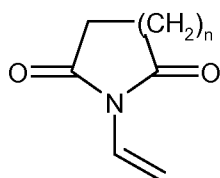


10 Formula (III)

wherein n is 1, 2 or 3. Examples of a monomer of Formula (III) include N-vinylcaprolactam, N-vinylvalerolactam and N-vinylbutyrolactam, (also known as N-vinylpyrrolidone);

15

A4. N-vinyl imides of Formula (IV)

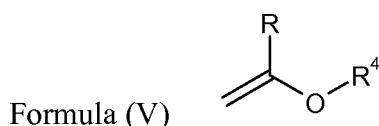


Formula (IV)

wherein n is 1, 2 or 3.

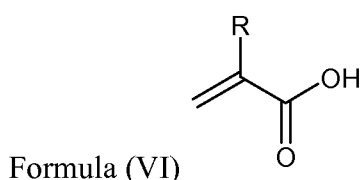
- 20 Examples of a monomer of Formula (IV) include N-vinylsuccinimide and N-vinylphthalimide;

A5. Vinyl ethers of Formula (V)



wherein R is as hereinbefore defined and R⁴ is a C₁-C₂₀ alkyl group. Examples of a monomer of Formula (V) include methyl vinyl ether, ethyl vinyl ether, propyl vinyl ether, and butyl vinyl ether;

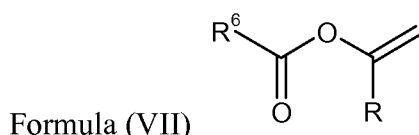
B1. Vinyl carboxylic acids or salts or esters thereof, of Formula (VI)



wherein R is as hereinbefore defined.

Suitable salts include alkali metal salts, such as sodium or potassium or an ammonium salt. Suitable esters include C₁-C₆ alkyl esters wherein the alkyl group is optionally substituted by -N(R⁵)₂ wherein each R⁵ which may be the same or different is selected from H or C₁-C₆ alkyl. Examples of monomers of Formula (VI) include acrylic acid, itaconic acid, methacrylic acid, methyl acrylate, ethyl acrylate, propyl acrylate, butyl acrylate, methyl methacrylate, ethyl methacrylate, sodium acrylate and (2-diethylamino)ethyl methacrylate;

B2. O-vinyl esters of Formula (VII)



wherein R is as hereinbefore defined and R⁶ is a C₁-C₁₁ alkyl group. Examples of a monomer according to Formula (VII) include vinyl acetate, vinyl propanoate and vinyl butanoate.

Suitably the homo or co-polymer microgels comprise at least one monomer selected from a vinyl amide of Formula (I), a vinyl ester of Formula (II), an N-vinyl lactam of Formula (III), an N-vinyl imide of Formula (IV), a vinyl ether of Formula (V), a vinyl carboxylic acid or salt or ester thereof of Formula (VI), and an O-vinyl ester of Formula

(VII) In one embodiment the homo or co-polymer microgels comprise at least one monomer selected from a vinyl amide of Formula (I), an N-vinyl lactam of Formula (III) and a vinyl carboxylic acid or salt or ester thereof of Formula (VI). In one embodiment the co-polymer microgels comprise a monomer selected from a vinyl amide of Formula (I) and
5 a monomer selected from a vinyl carboxylic acid or salt or ester thereof of Formula (VI); a monomer selected from an N-vinyl lactam of Formula (III) and a monomer selected from a vinyl carboxylic acid or salt or ester thereof of Formula (VI); and a combination of two different monomers selected from a vinyl carboxylic acid or salt or ester thereof of Formula (VI). In one embodiment the homo or co-polymer microgels comprise at least one
10 monomer selected from N-isopropylacrylamide, N-vinylcaprolactam and methyl methacrylate. In one embodiment the co-polymer microgels are selected from poly(N-isopropylacrylamide/acrylic acid, poly(N-vinylcaprolactam/methyl methacrylate) and poly(methyl methacrylate/methacrylic acid). Suitably when the monomer comprises an alkyl(meth)acrylate component, a co-monomer does not comprise a styrene sulfonic acid
15 component.

The term 'C₁-C₆ alkyl' as used herein as a group or a part of the group refers to a linear or branched alkyl group containing from 1 to 6 carbon atoms; examples of such groups include methyl, ethyl, propyl, isopropyl, n-butyl, isobutyl, tert butyl, pentyl or hexyl.

20 The term 'C₁-C₁₁ alkyl' as used herein as a group or a part of the group refers to a linear or branched alkyl group containing from 1 to 11 carbon atoms;

The term 'C₁-C₂₀ alkyl' as used herein as a group or a part of the group refers to a linear or branched alkyl group containing from 1 to 20 carbon atoms;

Suitably in one aspect a thermally responsive microgel for use in the invention will
25 comprise from about 60-100% by weight, in particular 90-100% of monomer(s) A and from 0-40% by weight, in particular 0-10%, of monomer(s) B.

Suitably in one aspect a pH responsive microgel for use in the present invention will comprise from about 60-100% by weight, in particular 90-100% of monomer(s) A and from 0-40% by weight, in particular 0-10%, of monomer(s) B.

30 In an alternative aspect a pH responsive microgel for use in the invention will suitably comprise 100% by weight of monomer(s) B selected from B1 esters.

Suitably in one aspect a non responsive microgel for use in the invention will comprise from about 60-100% by weight, in particular 90-100% of monomer(s) A and

from 0-40% by weight, in particular 0-10%, of monomer(s) B and will be employed when the microgel will not be exposed to the appropriate triggers of a physical conformational change. The properties of the microgels used in the invention will depend, among other factors, on the nature and concentration of the monomer(s), the cross-linking agent and initiator used and on the reaction temperature. It will be appreciated that any given microgel may be pH responsive and/or thermally responsive and/or non-responsive depending upon the environmental conditions it is exposed to.

Microgel particles of use in the invention have a surface charge. Reaction initiators for use in the preparation of the microgel particles are radical reaction initiators and provide a source of the surface charge. Suitable reaction initiators are described in the polymer art. A water-soluble initiator is preferred, for example a persulphate salt such as ammonium, sodium or potassium persulphate; 2,2-azobis(amidinopropane) dihydrochloride; dibenzoyl peroxide; 2,2-azobisisobutyronitrile and 4,4'-azobis(4-cyanovaleric acid). In one embodiment the reaction initiator is a persulphate salt such as potassium persulphate. A persulphate salt is a source of sulphate radicals which provide a surface charge. In an alternative embodiment the reaction initiator is 4,4'-azobis(4-cyanovaleric acid). Suitably in one aspect 1-30 wt % of initiator can be employed to prepare all types of microgels, in particular 5-15 wt %.

It is essential that the polymers for use as microgels in the invention are cross-linked. This can be achieved by the use of a suitable crosslinking agent for example a self-crosslinking monomer/co-monomer and/or a cross-linking reagent. Suitable cross-linking reagents for use in the preparation of the microgels are also described in the polymer art. Cross-linking molecules contain two vinyl groups and can include cross-linking monomers such as N,N-methylenebisacrylamide, ethyleneglycol dimethacrylate, divinyl sulfone, divinyl benzene, divinyl ether. In one embodiment the cross-linking agent is N,N-methylenebisacrylamide. Suitably in one aspect 1-40 wt % of cross-linking monomer can be employed to prepare all types of microgel particles, in particular 5-20 wt %.

Methods known in the art for preparing microgels include emulsion polymerisation, inverse emulsion polymerisation, living free-radical polymerisation and synthesis by radiation. A widely used method for the synthesis of microgels is surfactant-free emulsion polymerisation (SFEP) which generally involves:

- 1). Preparing an aqueous solution of a suitable initiator e.g. dissolving potassium persulphate in water at a concentration of 0.5g / 100ml, and heating to about 70°C;
- 2). In a separate vessel preparing an aqueous solution of a suitable monomer e.g. “monomer A” e.g. N-isopropylacrylamide (5g), and (if used) a co-monomer e.g. acrylic acid and, (if used) a suitable cross-linking reagent (e.g. N’N-methylenebisacrylamide) (0.5g);
- 3). Adding 2 to 1 and allowing the reaction to proceed at a suitable temperature e.g. 70°C, in an inert atmosphere e.g. under nitrogen, for a suitable period of time e.g. up to about 6 hours;
- 4). Cooling down and then purifying the reaction mixture e.g. by dialysing for a suitable time period e.g. for about seven days, and then recovering the microgel dispersion formed.
- 5). Optionally freeze drying or spray drying the microgel dispersion, as may desired.

Suitably microgel particles of use herein comprise good adhesion properties and the particles may be retained for a period of time, for example for up to an hour or longer for example up to twelve hours, within the oral cavity, following administration thereto. Whilst microgel particles for use in the invention are naturally bioadhesive, their bioadhesiveness may be enhanced by the selection of particular reactants or combinations thereof e.g. monomers and/or reaction initiators, that comprise specifically an anionic functional group. For example by the selection of a monomer comprising a carboxylate functional group e.g. a vinyl carboxylic acid of Formula (VI), or a reaction initiator comprising a sulphate group e.g. a persulphate salt. In a further embodiment microgel particles for use in the invention comprise an anionic functional group such as a carboxylate or a sulphate.

Poly(NIPAM)microgels are by far the most widely investigated and reported homopolymer microgel systems, and are of particular interest herein because they show a thermo-reversible conformational transition in water at a temperature of about 34°C. Copolymer microgels employing NIPAM are also widely studied and reported and exhibit a thermo-reversible transition in water at above or below 34°C depending on the comonomer and the amount of co-monomer employed. The more hydrophilic the comonomer, the higher the VPTT, and the more hydrophobic, the lower the VPTT. For example in one embodiment a poly(NIPAM/acrylic acid) microgel undergoes a volume phase transition at a temperature of about 35°C.

In one aspect according to the invention there is provided an oral care composition comprising microgel particles selected from poly(NIPAM) and poly(NIPAM/acrylic acid). In one embodiment according to the invention there is provided an oral care composition comprising thermally responsive microgel particles selected from poly(NIPAM) and
5 poly(NIPAM/acrylic acid) wherein the said microgel particles undergo a volume phase transition at a temperature in the range of from about 30 to about 40°C.

Other examples of suitable microgel particles for use in the invention include homo- and co-polymer microgels of N-vinylcaprolactam, in the presence or absence of a suitable co-monomer. N-vinylcaprolactam microgel particles undergo a thermoreversible
10 volume phase transition in water in a range of from about 30°C to about 40°C. In one aspect according to the invention there is provided an oral care composition comprising microgel particles selected from homo or co-polymer microgels of N-vinylcaprolactam. In one embodiment according to the invention there is provided an oral care composition comprising thermally responsive N-vinylcaprolactam microgel particles wherein the said
15 microgel particles undergo a volume phase transition at a temperature of from about 30 to about 40°C.

Particular microgel particles may be triggered to undergo a physical conformational change by more than one trigger or stimulus. For example poly(NIPAM/acrylic acid) (identified hereinabove as being thermally responsive) may under certain conditions be
20 responsive to changes in temperature and/or pH. When the pH of a dispersion of poly(NIPAM/acrylic acid) microgel particles is adjusted from below pH 4 to above pH 4.5 i.e. from below to above the pK_a of acrylic acid, the microgel particles therein will undergo a physical conformational change. Accordingly in one aspect according to the invention, there is provided an oral care composition comprising poly(NIPAM/Acrylic
25 acid) microgel particles such that the microgel particles therein undergo a volume phase transition in response to a change in pH i.e. at the pK_a of acrylic acid.

One example of a non-responsive co-polymer based microgel system is poly(methylmethacrylate/methylacrylic acid). Accordingly there is provided an oral composition wherein the non-responsive microgel particles comprises
30 poly(methylmethacrylate/methylacrylic acid).

An oral care composition according to the invention will suitably comprise from about 0.01% to 20.00% w/w of microgel particles, preferably from about 0.1% to about

5.00%w/w, even more preferably from about 0.50% to about 2.00% by weight of the composition.

Compositions of the present invention contain one or more orally acceptable carriers or excipients. Such carriers and excipients include appropriate formulating agents such as abrasives, surfactants, thickening agents, humectants, flavouring agents, sweetening agents, opacifying or colouring agents, pH buffering agents and preservatives, selected from those conventionally used in the oral care composition art for such purposes. Examples of such agents are as described in EP 929287.

The oral compositions of the present invention are typically formulated in the form of toothpastes, sprays, mouthwashes, gels, suspensions, varnishes, sealants, coatings, lozenges, chewing gums, tablets, pastilles, instant powders, oral strips and buccal patches.

The efficacy of oral care compositions comprising microgels according to the invention may be further enhanced by inclusion of a nerve-desensitising agent such as described in WO 02/15809. Suitable desensitising agents include a potassium salt such as potassium citrate, potassium chloride, potassium bicarbonate, potassium gluconate, and especially potassium nitrate. The compositions of the present invention may also contain additional occlusion agents whose mode of action involves reaction in situ such as strontium salts of chloride, acetate or nitrate, calcium and phosphate ion sources and stannous salts. Additional passive occlusion agents that may be incorporated into the compositions of the present invention include silicas, titanium oxide and organic thickening systems such as cellulose polymers, guar gums and polyacrylic acid or any of the tubule occluding agents referenced in WO02/15809.

Compositions of the present invention may further comprise a source of soluble fluoride ions such as those provided by sodium fluoride, sodium monofluorophosphate, tin (II) fluoride or an amine fluoride in an amount to provide from 0.1 to 3500 ppm fluoride, such as from 100 to 1500 ppm.

Compositions according to the present invention may be prepared by admixing the ingredients in the appropriate relative amount in any order that is convenient.

The present invention also provides a method of combating dentine hypersensitivity which comprises applying an effective amount of a composition as herein before defined to an individual in need thereof.

The invention is further illustrated by the following Examples:

Microgel Synthesis

Example 1

5 **The preparation of a poly(N-isopropylacrylamide/acrylic acid) microgel**

All of the following reactions were carried out in a fume cupboard. The reaction procedure for the synthesis of a copolymer poly(N-isopropylacrylamide/acrylic acid) [p(NIPAM/AAc)] microgel prepared by surfactant free emulsion polymerisation (SFEP) was as follows: 4.5 g NIPAM, 0.5 g AAc, and 0.5 g N,N-methylenebisacrylamide (BA) were dissolved in 200 mL distilled water with constant stirring for 30 min. 0.5g potassium persulphate (KPS) was dissolved in 800 mL distilled water in a 2 L reaction vessel to which a 5 neck lid was fitted and clamped shut. The KPS solution was then heated to 70°C, with constant stirring, using a feedback hotplate stirrer. A temperature probe was inserted into the solution through the neck of the flask to monitor and control the temperature of the solution. The reaction vessel was fitted with a condenser, and a pressure equalising separating funnel. The monomer and cross-linker solution was placed in the separating funnel and nitrogen gas was passed through the system. When the temperature of the KPS solution reached 70°C, the monomer solution was added via the separating funnel and the reaction was left to proceed for 6 hours with constant stirring. After reaction completion, the final product was cooled to room temperature and filtered through glass wool to remove large molecular weight impurities. The microgel was then placed in dialysis bags with a 12 kD molecular weight cut-off and left to dialyse for 7 days against distilled water to remove any un-reacted monomer and other impurities from the dispersion. The dialysate was changed once a day until a conductivity value of 1 μ S was obtained.

Example 2

30 **The preparation of a poly(N-vinylcaprolactam/methyl methacrylate) microgel**

All of the following reactions were carried out in a fume cupboard. The reaction procedure for the synthesis of a copolymer poly(N-vinylcaprolactam/methyl methacrylate) [p(NVCL/MMA)] microgel prepared by surfactant free emulsion polymerisation (SFEP) is as follows: 4.0 g NVCL, 1.0 g MMA, and 1.0 g N,N-methylenebisacrylamide (BA) were

dissolved in 200 mL distilled water with constant stirring for 30 min. 0.5g 2,2'-azobis(2-methylpropionamidine) dihydrochloride (AMPD) was dissolved in 800 mL distilled water in a 2 L reaction vessel to which a 5 neck lid was fitted and clamped shut. The AMPD solution was then heated to 70°C, with constant stirring, using a feedback hotplate stirrer.

5 A temperature probe was inserted into the solution through the neck of the flask to monitor and control the temperature of the solution. The reaction vessel was fitted with a condenser, and a pressure equalising separating funnel. The monomer and cross-linker solution was placed in the separating funnel and nitrogen gas was passed through the system. When the temperature of the AMPD solution reached 70°C, the monomer
10 solution was added via the separating funnel and the reaction was left to proceed for 6 hours with constant stirring. After reaction completion, the final product was cooled to room temperature and filtered through glass wool to remove large molecular weight impurities. The microgel was then placed in dialysis bags with a 12 kD molecular weight cut-off and left to dialyse for 7 days against distilled water to remove any un-reacted
15 monomer and other impurities from the dispersion. The dialysate was changed once a day until a conductivity value of 1 μ S was obtained. The microgel concentration was increased by reverse dialysis, using 12kD molecular weight cut-off dialysis bags and high molecular weight (20,000g/mol) polyethylene glycol (PEG).

Alternatively the microgel solution may be purified by increasing the ionic strength with
20 the addition and dissolving of a salt, the preferred salt being sodium chloride at a level of around 0.5%. The solution can then be warmed to above around 40°C and the ion presence initiates the conformational changes in the polymer resulting in aggregation and sedimentation. The supernatant can be removed with a residual concentrate remaining. This can then be further diluted with salt solution if required and the process repeated. This
25 has this advantage of both enabling the preparation of concentrated microgel solutions and also the removal of dissolved residual monomers.

Example 3

30 The preparation of a poly(methyl methacrylate/methacrylic acid) microgel

All of the following reactions were carried out in a fume cupboard. The reaction procedure for the synthesis of a copolymer poly(methyl methacrylate/methacrylic acid) [p(MMA/MAAc)] microgel prepared by surfactant free emulsion polymerisation (SFEP)

was as follows: 8.0 g MMA, and, 2.0 g MAAC, 0.5 g N,N-methylenebisacrylamide (BA) were dissolved in 200 mL distilled water with constant stirring for 30 min. 1.0 g 2,2-azobis(cyanovaleric acid) (ACA) was dissolved in 800 mL distilled water in a 2 L reaction vessel to which a 5 neck lid was fitted and clamped shut. The ACA solution was then heated to 70°C, with constant stirring, using a feedback hotplate stirrer. A temperature probe was inserted into the solution through the neck of the flask to monitor and control the temperature of the solution. The reaction vessel was fitted with a condenser, and a pressure equalising separating funnel. The monomer and cross-linker solution was placed in the separating funnel and nitrogen gas was passed through the system. Figure 1 illustrates the reaction setup. When the temperature of the ACA solution reached 70°C, the monomer solution was added via the separating funnel and the reaction was left to proceed for 6 hours with constant stirring. After reaction completion, the final product was cooled to room temperature and filtered through glass wool to remove large molecular weight impurities. The microgel was then placed in dialysis bags with a 12 kD molecular weight cut-off and left to dialyse for 7 days against distilled water to remove any un-reacted monomer and other impurities from the dispersion. The dialysate was changed once a day until a conductivity value of 1 μ S was obtained.

Characterisation of Microgels

Example 4

Turbidimetric analysis

Turbidimetric analysis of the microgels has been carried out over a temperature or pH range to determine the temperature or pH at which the VPT occurs. The percentage of transmitted light at 547 nm versus temperature or pH for each microgel is used to determine the VPT for each microgel. The first derivative is the change in transmittance at each point, plotted against the corresponding change in temperature or pH. This enables the determination of the temperature or pH where the largest change in transmittance occurs, and therefore the VPTT or the VPpK respectively. Figures 1 and 2 show the percentage (%) transmittance and first derivative respectively for poly(NIPAM/AAc) and poly(NVCL/MMA).

Example 5

Dynamic light scattering (DLS)

5 The hydrodynamic diameter of microgel particles was measured using a Malvern Zetasizer Nano ZS, equipped with a 4 mW He-Ne laser ($\lambda = 633$ nm) with the detector positioned at 173° to the sample. The dispersion temperature was maintained by peltier thermocouple, and the samples were equilibrated at each temperature for 15 minutes before data collection. All microgel dispersions were analysed as a function of temperature (20-50 °C
10 at 5 °C intervals). Selected microgels were analysed as a function of pH (2,4,6,8, and 10). Microgel particle size was measured in the presence of Earle's solution at pH 2,4,6, and 8 for each microgel to determine the stability of the microgel in electrolyte and give an indication of dispersion stability The overall stability of each dispersion in Earle's solution was determined by a combination of DLS and visual observation. Figures 3 shows the
15 particle size versus temperature for poly(NIPAM/AAc) and poly(NVCL/MMA) and Figure 4 shows the particle size versus pH for poly(NIPAM/AAc).

Example 6

20 Hydraulic conductance testing

Briefly, dentine permeability as a function of hydraulic conductance (the flow of Earls solution through a dentine disc) was measured for each specimen (dentine disc) at baseline and after treatment. Thereby, each disk served as its own control. Prior to treatment the
25 hydraulic conductance of each specimen was measured. This value was set to represent 100% permeability, and is termed the initial flow of the disk. Hydraulic conductance measurements have been carried out using two methods.

Method One

30 In Method One, hydraulic conductance experiments were carried out at room temperature. Microgel samples were heated to 45°C (above the VPTT) and then applied to a dentine disc, which was kept at room temperature. Figures 5 and 6 show the reduction in the flow of Earls solution through the dentine disc following the baseline measurement (INITIAL), 3 subsequent treatments with
35 poly(NIPAM/AAc), (T1-T3) and rinses with water (R1-R3). A treatment consisted of

application of the test active to the dentine disc and the hydraulic conductance was re-measured at one minute intervals (over 5 minute time period). The value obtained was used to calculate a percentage permeability reduction for the particular test active. The rinse step involved washing the treated dentine surface with water for 1 minute. Following treatments and rinses the disks were subjected to simulated oral challenges. In order, these consisted of (i) a 30 sec brush (BRUSH) (ii) the application of a 10 sec. purge pressure (10 p.s.i. on the pulpal side of the disk) (PURGE).

Method Two

In Method Two, hydraulic conductance experiments were carried out at 35-36°C and 70% relative humidity in order to simulate conditions in the oral cavity. Microgel samples were applied at room temperature and then heated when in contact with the dentine disc and Earls solution. Figures 7 and 8 show the reduction in the flow of Earls solution through the dentine disc following the baseline measurement (INITIAL), 3 subsequent treatments with poly(NIPAM/AAc) poly(NVCL/MAA) (T1-T3) (respectively) and rinses with water (R1-R3). A treatment consisted of application of the test active to the dentine disc and the hydraulic conductance was re-measured at one minute intervals (over 5 minute time period). The value obtained was used to calculate a percentage permeability reduction for the particular test active. The rinse step involved washing the treated dentine surface with water for 1 minute. Following treatments and rinses the disks were subjected to simulated oral challenges. In order, these consisted of (i) a 30 sec brush (BRUSH) (ii) the application of a 10 sec. purge pressure (10 p.s.i. on the pulpal side of the disk) (PURGE).

Table 1. Summary of Hydraulic conductance data for microgels tested on bovine dentine using Method One

Microgel	Trigger	Mechanism of occlusion	Hc data (% reduction in fluid flow w.r.t saliva baseline). SD in parentheses.		
			Initial reduction in Hc	% red. in Hc after 3 applications	% red. in Hc on (a) brushing, (b) purge.
Poly(NIPAM/AAc) 2 wt %	Thermal (VPTT 35°C)	Applied when $T > VPTT$, microgels (collapsed) swell in tubule when $T < VPTT$	63.9 (2.0)	88.3 (2.3)	(a) 77.8(2.8) (b) 90.0 (1.52)
Poly(MMA/MAAc) 2 wt %	Non-responsive	Particles block tubule	68.2 (5.3)	87.1 (2.6)	(a) 94.1 (b) not carried out

5

Table 2. Summary of Hydraulic conductance data for microgels tested on bovine dentine using Method Two.

Microgel	Trigger	Mechanism of occlusion	Hc data (% reduction in fluid flow w.r.t saliva baseline). SD in parentheses.		
			Initial reduction in Hc	% red. in Hc after 3 applications	% red. in Hc on (a) brushing, (b) purge.
Poly(NIPAM/AAc) 2 wt %	Thermal (VPTT 35°C)	Applied when $T < VPTT$. (swollen) Microgels collapse flocculate in tubule when $T > VPTT$	24.4 (9.3)	77.8 (7.9)	(a) 53.3 (2.2) (b) 73.3 (6.1)
Poly(NVCL/MMA) 0.5 wt %	Thermal (VPTT 35.5°C)	Applied when $T < VPTT$ (swollen). Microgels collapse and flocculate in tubule when $T > VPTT$	30.1 (1.8)	26.5 (0.4)	(a) 33.7 (1.9) (b) 55.4 (1.5)

10

Conclusion

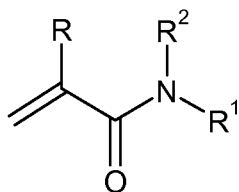
Microgels have been synthesised and characterised with respect to particle size and volume phase transition behaviour. Microgels which undergo a volume phase transition (VPT) in response to changing temperature have shown ability to occlude dentine tubules the mechanism of which is thought to be flocculation or swelling in tubules. Non-responsive microgels have also demonstrated the ability to occlude tubules, the mechanism of which is thought to be by the particles blocking the tubules, the effect of which is enhanced by the presence of carboxyl groups which possess a good affinity for dentine.

CLAIMS

1. An oral care composition comprising a dispersion of responsive or non-responsive microgel particles, and at least one orally acceptable carrier or excipient for treating dentine hypersensitivity and wherein the responsive microgel particles undergo a physical conformational change in response to a trigger selected from temperature and/or pH.
2. An oral care composition according to claim 1 comprising responsive microgel particles.
3. An oral care composition according to claim 1 or claim 2 wherein the responsive microgel particles are thermally responsive and the trigger is temperature.
4. An oral care composition according to claim 3 wherein the physical conformational change of the thermally responsive microgel particles comprises a volume phase transition occurring at the volume phase transition temperature of the said particles.
5. An oral care composition according to claim 4 wherein the thermally responsive microgel particles undergo a volume phase transition occurring at a volume phase transition temperature in the range of from about 30°C to about 50°C, optionally in the range from about 32°C to about 38°C.
6. An oral care composition according to claim 4 or claim 5 wherein the volume phase transition comprises a transition from a swollen state to a collapsed state, followed by flocculation.
7. An oral care composition according to claim 3 wherein the thermally responsive microgel particles undergo a volume phase transition at a volume phase transition temperature which is higher than the temperature of the oral cavity, and is suitably in the range of from about 39°C to about 45°C, such that on heating of the composition to the volume phase transition temperature or above, the microgel particles undergo a reversible first volume phase transition and then on cooling to below the volume phase transition temperature the microgel particles undergo a second volume phase transition.

8. An oral care composition according to claim 7 wherein the first volume phase transition is from a swollen state to a collapsed state and the second volume phase transition is from the collapsed state to the swollen state.
9. An oral care composition according to claim 1 or claim 2 wherein the responsive microgel particles are pH responsive and the trigger is pH.
10. An oral care composition according to claim 9 wherein the physical conformational change of the pH responsive microgel particles comprises a volume phase transition occurring at the VPpKa of the said particles.
11. An oral care composition according to any one of claims 1 to 10 wherein the said microgel particles comprise a polymeric network comprising one or more monomers A selected from A1 to A5:

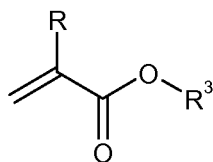
A1. Vinyl amides of Formula (I)



Formula (I)

wherein R is H or C₁-C₆ alkyl, and R¹ and R² which may be the same or different are selected from H or C₁-C₆ alkyl optionally substituted by hydroxy or C₁-C₆ alkoxy;

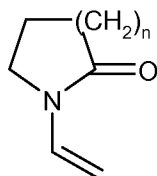
A2. Vinyl esters of Formula (II)



Formula (II)

wherein R is as hereinbefore defined and R³ is C₁-C₆ alkyl substituted by hydroxy.

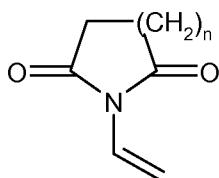
A3. N-vinyl lactams of Formula (III)



Formula (III)

wherein n is 1, 2 or 3

A4. N-vinyl imides of Formula (IV)

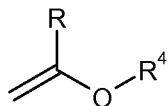


Formula (IV)

5

wherein n is 1, 2 or 3;

A5. Vinyl ethers of Formula (V)

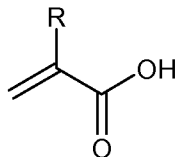


Formula (V)

10

wherein R is as hereinbefore defined and R⁴ is a C₁-C₂₀ alkyl group;
and/or one or more monomers B selected from B1 to B3:

B1. Vinyl carboxylic acids or salts or esters thereof, of Formula (VI)

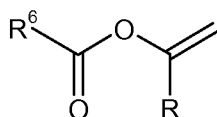


Formula (VI)

15

wherein R is as hereinbefore defined.

B2. O-vinyl esters of Formula (VII)



Formula (VII)

20

wherein R is as hereinbefore defined and R⁶ is a C₁-C₁₁ alkyl group.

12. An oral care composition according to claim 11 wherein the monomers A1 are selected from N-ethylacrylamide, N-isopropylacrylamide and N,N-dimethylacrylamide.

13. An oral care composition according to claim 11 wherein the monomers A2 are selected from hydroxyethyl acrylate, hydroxyethyl methacrylate, hydroxylpropyl acrylate, hydroxypropyl methacrylate and hydroxybutyl acrylate.
14. An oral care composition according to claim 11 wherein the monomers A3 are selected from N-vinylcaprolactam, N-vinylvalerolactam and N-vinylbutyrolactam, (also known as N-vinylpyrrolidone).
15. An oral care composition according to claim 14 wherein the monomer comprises N-vinylcaprolactam.
16. An oral care composition according to claim 11 wherein the monomers A4 are selected from N-vinylsuccinimide and N-vinylphthalimide.
17. An oral care composition according to claim 11 wherein the monomers A5 are selected from methyl vinyl ether, ethyl vinyl ether, propyl vinyl ether, and butyl vinyl ether.
18. An oral care composition according to claim 11 wherein the monomers B1 are selected from acrylic acid, itaconic acid, methacrylic acid, methyl acrylate, ethyl acrylate, propyl acrylate, butyl acrylate, methyl methacrylate, ethyl methacrylate, sodium acrylate and (2-diethylamino)ethyl methacrylate.
19. An oral care composition according to claim 11 wherein the monomers B2 are selected from vinyl acetate, vinyl propanoate and vinyl butanoate.
20. An oral care composition according to any one of claims 1 to 10 wherein the responsive microgel particles comprise poly(NIPAM)/AAc microgel particles.
21. An oral care composition according to any one of claims 1 to 10 wherein the responsive microgel particles comprise poly(NVCL)/MMA microgel particles.
22. An oral care composition according to claim 1 wherein the microgel particles are non-responsive microgel particles.
23. An oral care composition according to any one of claims 1 to 22 comprising an oral active agent.
24. An oral care composition according to claim 23 wherein the oral active agent includes a desensitizing agent.
25. A method of treating dentine hypersensitivity comprising applying an effective amount of a composition as claimed hereinbefore to an individual in need thereof.

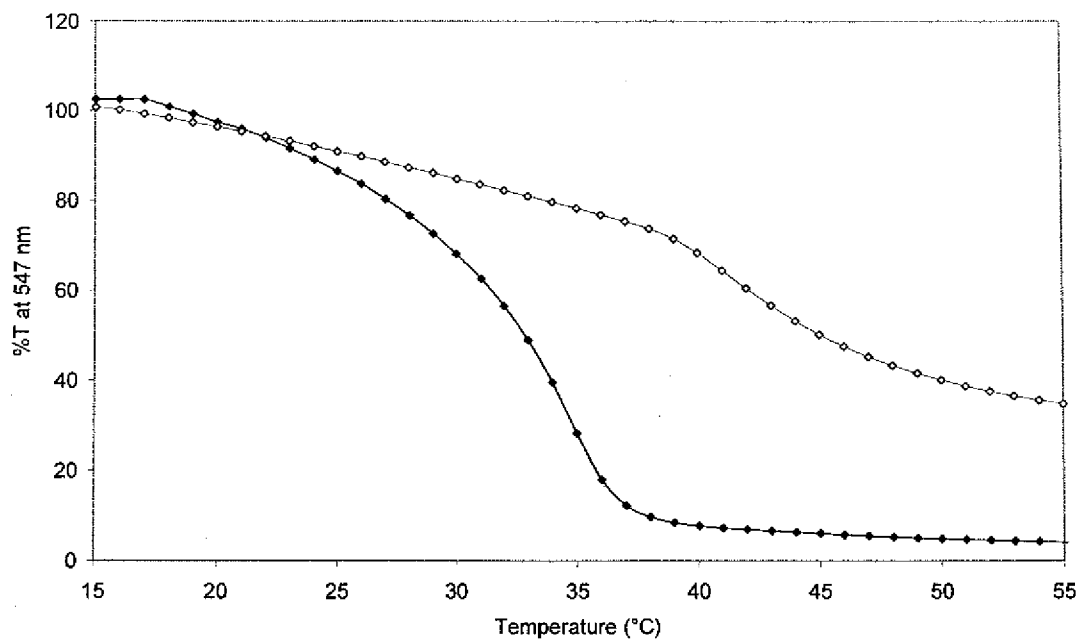


Figure 1

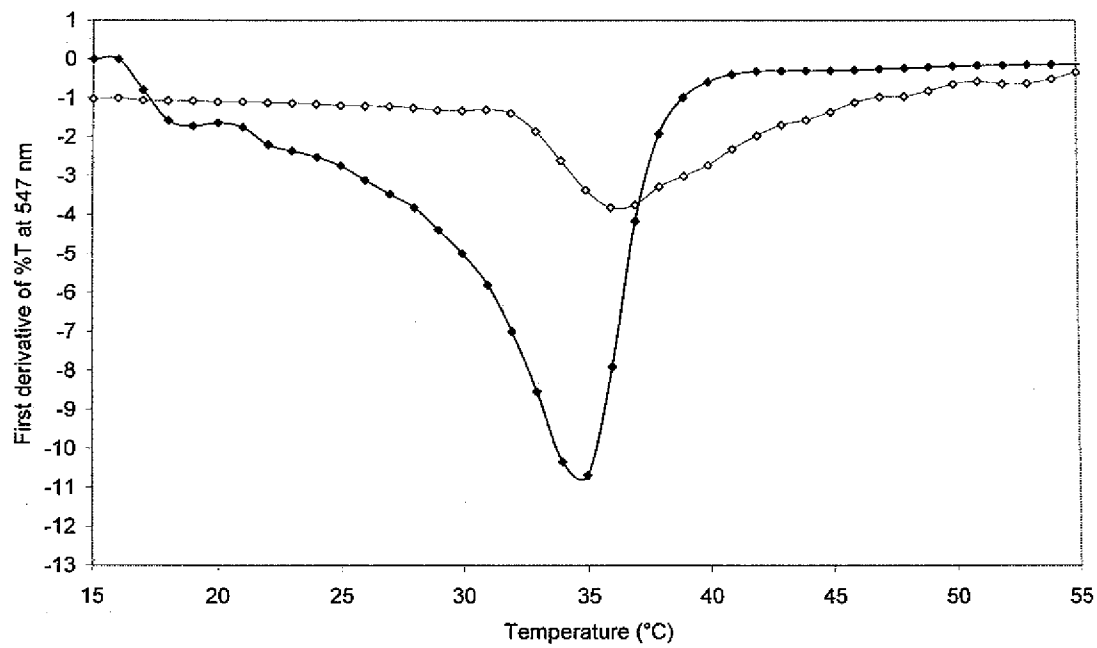


Figure 2

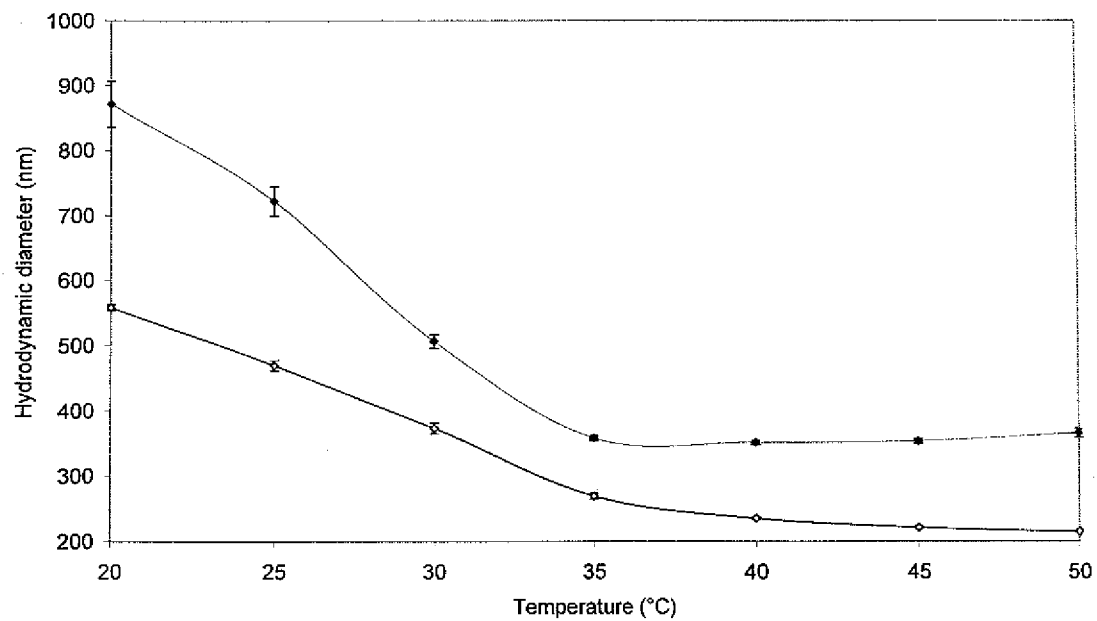


Figure 3

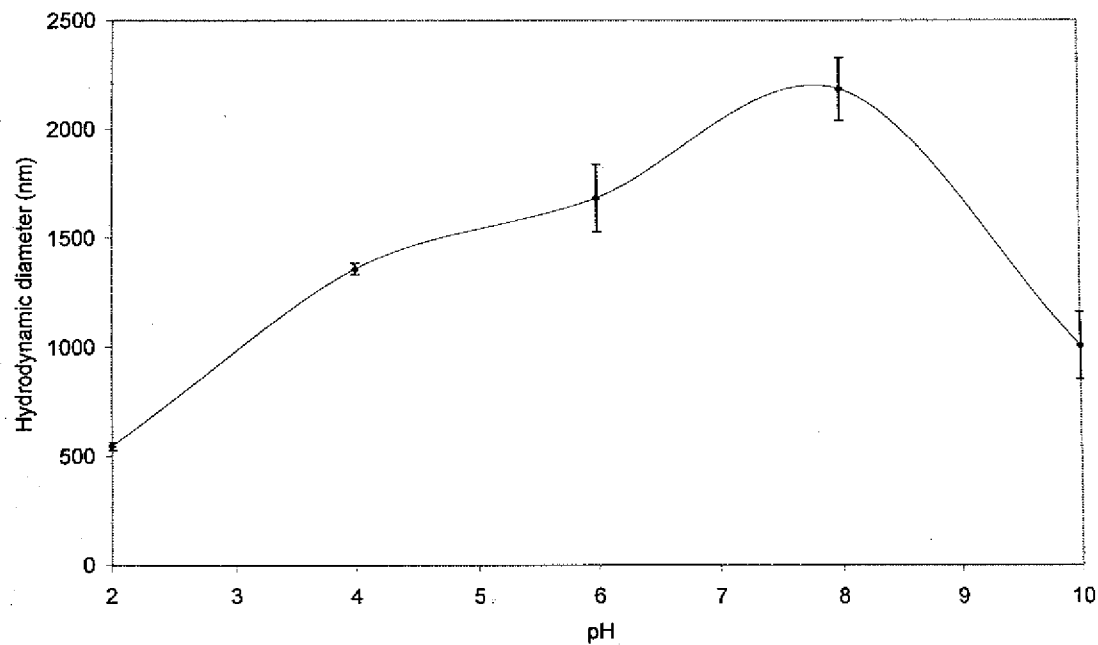


Figure 4

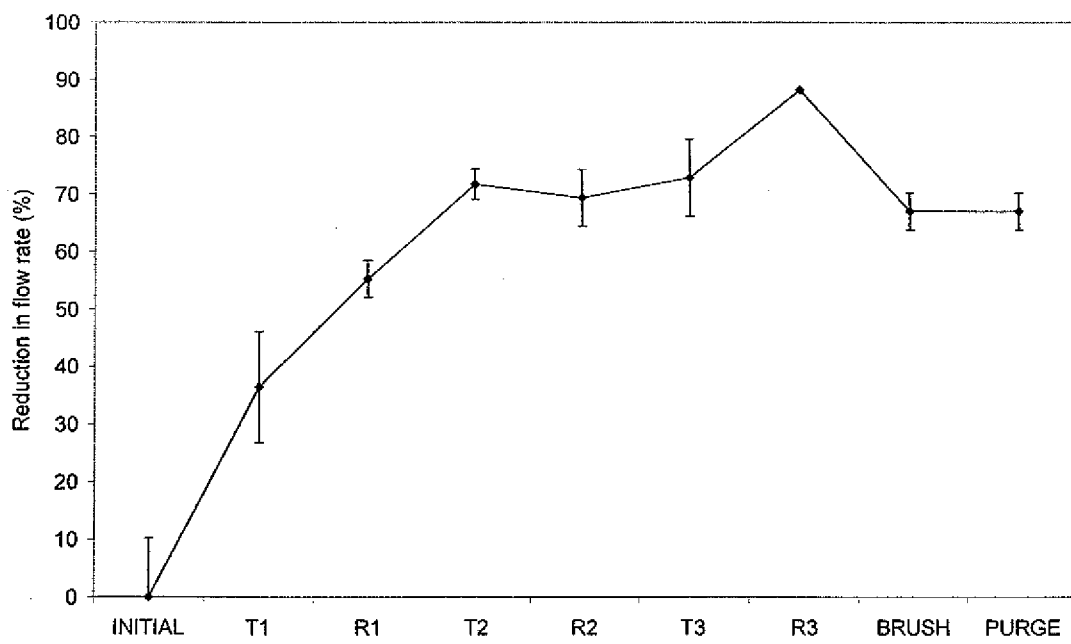


Figure 5

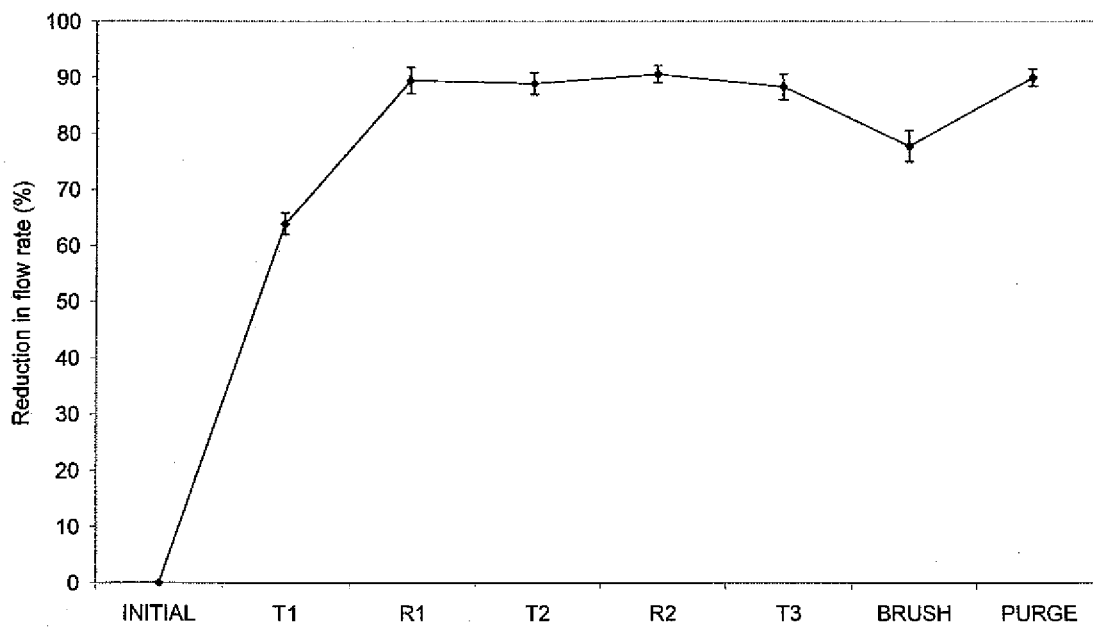


Figure 6.

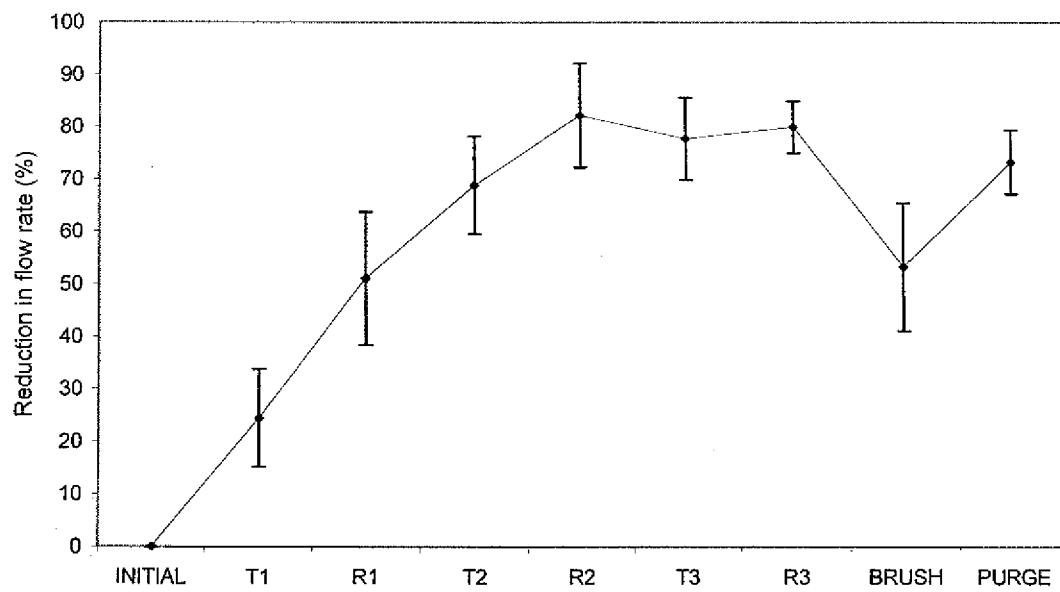


Figure 7.

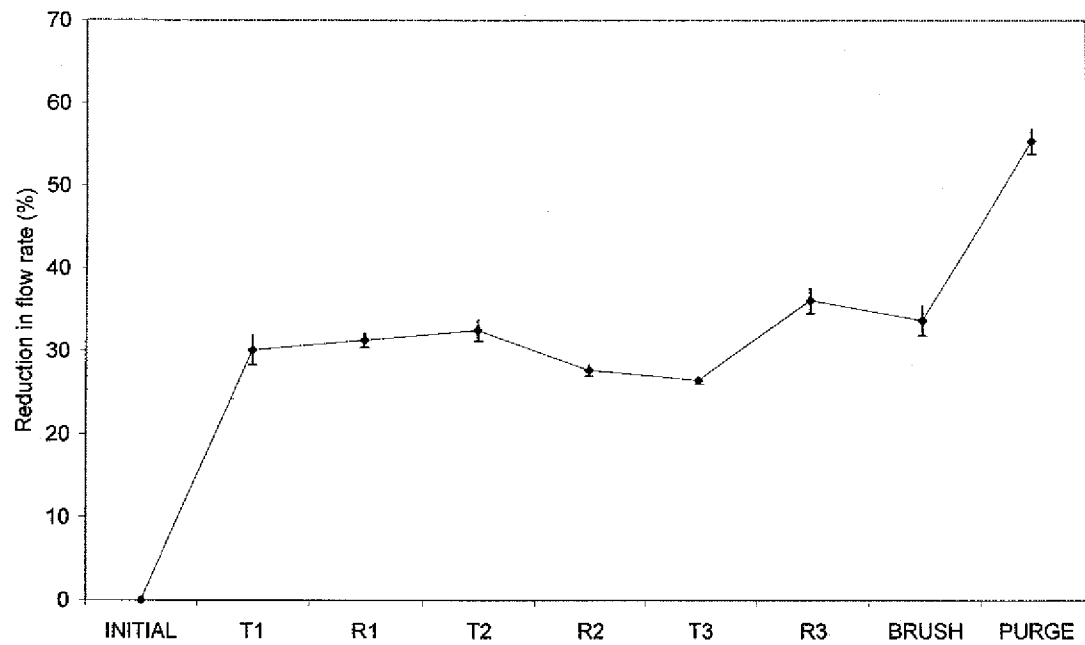


Figure 8